656. *The Structure of Tannins. Part I. The Reduction of Chalkone.*

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The bimolecular reduction product of chalkone obtained by Russell (*J.*, 1934, 218) has been shown by the preparation of a dioxime and by synthesis from ($\pm$)-$\beta\beta'$-diphenyladipoyl chloride and diphenylcadmium to be ($\pm$)-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione (II), and not a pinacol as suggested by Russell. Thus, there is no reason to believe that reduction of substituted chalkones gives " flavpinacols " and no basis for the assumption of such a structure in the tannins.

Some of the reactions of ($\pm$)-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione have been studied and the isomeric *meso*-compound obtained by other authors from chalkone has also been synthesised from *meso*-$\beta\beta'$-diphenyladipoyl chloride and diphenylcadmium.

THE " flavpinacol " structure proposed for natural phlobatannins (Russell and Todd, *J.*, 1934, 1066; Russell, *Chem. Reviews*, 1935, **17**, 155) is based on the belief that the bimolecular reduction product, m. p. 197°, obtained from chalkone by zinc dust and acetic acid is a pinacol, presumably (I). From this it is supposed that the crystalline reduction products of other chalkones are similar and " that in the case of 2-hydroxychalkones the reaction follows the same course and that the reduction products of these are likewise of the bis type."

(I.) $[\cdot CPh(OH)\cdot CH{:}CHPh]_2$ $(\cdot CHPh\cdot CH_2\cdot COPh)_2$ (II.)

Harries and Hübner (*Annalen*, 1897, **296**, 295) had previously obtained from chalkone a bimolecular reduction product, m. p. 270°, which they considered to be 1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione (II). This structure was supported by Wislicenus and Lehmann (*ibid.*, 1898, **302**, 195) who obtained a similar compound by reduction of 2 : 3-diphenyl-1 : 4-dibenzoylbutadiene. Similarly, Conant and Cutter (*J. Amer. Chem. Soc.*, 1926, **48**, 1016) obtained two isomeric products, m. p. 194° and 266°, by reduction of chalkone with vanadous chloride and considered that they were stereoisomers of (II). This is in agreement with Kohler and Thompson's finding (*ibid.*, 1937, **59**, 887) that reduction of $\alpha\beta$-unsaturated ketones with zinc and acid proceeds solely by 1 : 4-addition, and with the ready dehydration of the low-melting isomer (Conant and Cutter, *loc. cit.*). Similar products were also obtained by Shima (*Mem. Coll. Sci. Kyoto*, 1929, A, **12**, 327; *Brit. Abstr.*, 1930, *A*, 344) although he believed the low-melting isomer to be (I), whereas Dippy and Lewis (*Rec. Trav. chim.*, 1937, **56**, 1000) obtained " 1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione," m. p. 243°—apparently a mixture of the two stereoisomers. Takagi and Sakaguti (*J. Pharm. Soc. Japan*, 1938, **58**, 797; *Chem. Abstr.*, 1939, **33**, 2508) follow Shima in describing their low-melting material (m. p. 167—168°) as (I).

Both isomers, m. p. 196° and 269°, have now been obtained by reduction of chalkone with zinc dust and acid, although it was not possible to duplicate the high yield of the low-melting isomer reported by Russell (*J.*, 1934, 218). This isomer was recovered unchanged after treatment with phenyl *iso*cyanate or with 3 : 5-dinitrobenzoyl chloride under mild conditions.

The substance, m. p. 196°, did not react with permanganate in boiling acetone. This lack of reactivity and the formation of a dibromide from it and from its dehydration product (Conant and Cutter, *loc. cit.*; Russell and Todd, *loc. cit.*) are difficult to reconcile with structure (I).

Positive evidence for structure (II) has now been obtained by the preparation of an oxime from the low-melting reduction product, under the conditions used by Cook, Hewett, and Lawrence (*J.*, 1936, 71) for the oximation of hexahydroanthrone. The high-melting isomer formed a nitrogen-containing product under these conditions but this was not obtained pure.

Finally, (±)- and *meso*-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione have been obtained from (±)- and *meso*-ββ′-diphenyladipic acids of known configuration (Oomen and Vogel, *J.*, 1930, 2148), by treatment of the acid chlorides with diphenylcadmium. The diphenyladipic acids were prepared by electrolytic reduction of cinnamic acid (Wilson and Wilson, *Trans. Electrochem. Soc.*, 1943, **84**, 153), and the *meso*-acid chloride was obtained by Oomen and Vogel's method (*loc. cit.*). The (±)-acid formed a red product under these conditions but, by Bachmann and Wilds's procedure [*J. Amer. Chem. Soc.*, 1940, **62**, 2084; Johnson, " Organic Reactions," Vol. II, p. 138 (procedure II)], (±)-ββ′-diphenyladipoyl chloride was obtained and used without further purification.

The (±)- and *meso*-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-diones obtained in this way were identical with the chalkone reduction products, m. p. 196° and 269°, respectively.

Russell and Todd (*loc. cit.*) obtained two isomeric dehydration products, m. p. 112° and 178°, by the action of alcoholic sulphuric acid on (±)-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione, and Conant and Cutter (*loc. cit.*) obtained, by the action of sodium ethoxide, a product of m. p. 123°, which they describe as 1-benzoyl-2 : 4 : 5-triphenyl*cyclo*pentene. Acetic anhydride and sulphuric acid or 3 : 5-dinitrobenzoyl chloride and pyridine have now been found to give a dehydration product, m. p. 182°, probably identical with Russell and Todd's product of m. p. 178°. From its behaviour with permonophthalic acid and its reaction with bromine to form a dibromide of m. p. 178° identical with that formed from (±)-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione, this appears to be 1-benzoyl-2 : 4 : 5-triphenyl*cyclo*pentene. When (±)-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione is treated with sodium ethoxide the same compound is obtained, but the isomer of m. p. 123° is also formed, in amount depending upon the time of reaction. The higher-melting was also converted into the lower-melting isomer by sodium ethoxide. The two isomers might be *meso*- and racemic forms of 1-benzoyl-2 : 4 : 5-triphenyl*cyclo*pentene, but this is unlikely as *meso*-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione resists dehydration with acetic anhydride and sulphuric acid and with bromine forms the same compound as does the (±)-isomer (Conant and Cutter, *loc. cit.*). Hence, the lower-melting isomer is believed to be 1-benzoyl-2 : 3 : 5-triphenyl*cyclo*pentene, formed by migration of the double bond in the presence of sodium ethoxide. This structural difference is confirmed by the fact that bromination of the presumed 1-benzoyl-2 : 3 : 5-triphenyl*cyclo*pentene gives, not a dibromide, but a product which, although not completely purified, is clearly only a monobromide.

Experimental.

(M. p.s are uncorrected.)

Reduction of Chalkone.—Chalkone (5 g.) in acetic acid (15 ml.) and alcohol (100 ml.) was heated under reflux during the gradual addition (10 minutes) of zinc dust (2 g.). The hot solution was filtered. The reduction products separated on cooling. On treatment with boiling alcohol (100 ml.) the lower-melting reduction product dissolved and formed colourless needles, m. p. 191—194° (1·3 g.), on cooling. Recrystallisation from acetone or alcohol raised the m. p. to 195—196° [Found : C, 86·0; H, 6·4%; *M*, 389 (Rast). Calc. for $C_{30}H_{26}O_2$: C, 86·1; H, 6·3%; *M*, 418·5]. This substance did not react with potassium permanganate in boiling acetone, with phthalic anhydride in boiling toluene, or with phenyl *iso*cyanate in boiling benzene, and did not form a coloured salt with chromic acid. It was also recovered unchanged after treatment with 3 : 5-dinitrobenzoyl chloride in boiling benzene.

The material not extracted by alcohol (0·5 g.) formed colourless needles, m. p. 268—269°, from benzene. It was slightly soluble in alcohol, acetone, benzene, chloroform, carbon tetrachloride, or ether and did not react with acetic anhydride and sulphuric acid in the cold or on warming.

Preparation of Dioximes.—(*a*) The reduction product of m. p. 196° (0·5 g.) and hydroxylamine hydrochloride (0·8 g.) were suspended in pyridine (1·5 ml.) and heated on a boiling water-bath for 2 hours. After cooling and evaporation of the solvent, water (40 ml.) was added and the precipitate collected, crystallised from aqueous alcohol, and washed with hot water and dilute hydrochloric acid till free from pyridine (0·5 g.). Eight crystallisations from aqueous methanol gave 1 : 3 : 4 : 6-*tetraphenylhexane*-1 : 6-*dione dioxime*, colourless plates, m. p. 218—219° (18 mg.) (Found : N, 6·4. $C_{30}H_{28}O_2N_2$ requires N, 6·25%).

(*b*) The reduction product, m. p. 268—269° (0·2 g.), treated by the same method gave a crude dioxime (0·16 g.), m. p. 242—250°, raised by eight crystallisations from methanol, acetone and aqueous alcohol to 270° (depresssed to 243—247° by the reduction product, m. p. 268—269°). This product (3·5 mg.) was not quite homogeneous when viewed under the microscope but contained nitrogen (Lassaigne test).

meso-1 : 3 : 4 : 6-*Tetraphenylhexane*-1 : 6-*dione*.—Magnesium (2·5 g.) was allowed to react with bromobenzene (16 g.) in ether (125 ml.; dried with sodium), and when the reaction was complete cadmium chloride (14 g.; powdered, sieved, and dried 2 days at 100°) was added during 2 hours with mechanical stirring and cooling in ice. After a further 30 minutes' stirring the ice was replaced by a water-bath, and *meso*-$\beta\beta'$-diphenyladipoyl chloride (1·5 g.) in warm benzene (100 ml.; dried with sodium) added and the ether distilled off. The mixture was then stirred and refluxed for 2½ hours, whereafter crushed ice and 10% hydrochloric acid (50 ml.) were added during 20 minutes, with stirring. On steam-distillation, *meso*-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione (0·95 g.) solidified and was collected and washed with ether and sodium hydroxide solution. It formed colourless needles (from benzene), m. p. 269—270°, undepressed on admixture with the chalkone reduction product of m. p. 268—269° but depressed to 252—254° on admixture with *meso*-$\beta\beta'$-diphenyladipic acid, m. p. 270—271°.

(±)-1 : 3 : 4 : 6-*Tetraphenylhexane*-1 : 6-*dione*.—(±)-$\beta\beta'$-Diphenyladipoyl chloride was obtained from (±)-$\beta\beta'$-diphenyladipic acid (3·0 g.) in dry ether (7·5 ml.) and pyridine (1 drop) with thionyl chloride (2·5 ml.), first at room temperature and then at 40° (cf. Bachmann and Wilds, *loc. cit.*; Johnson, *loc. cit.*) and added in benzene (120 ml.) to the solution of diphenylcadmium prepared as described above. Working up as above gave (±)-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione (2·3 g.) which, after being washed with sodium hydroxide solution, crystallised from alcohol in colourless needles, m. p. 195—196° undepressed on admixture with the chalkone reduction product of m. p. 196°.

Dehydration of (±)-1 : 3 : 4 : 6-*Tetraphenylhexane*-1 : 6-*dione*.—(a) *With acetic anhydride and sulphuric acid.* (±)-1 : 3 : 4 : 6-Tetraphenylhexane-1 : 6-dione (0·25 g.) rapidly dissolved in acetic anhydride (5 ml.) on the addition of sulphuric acid (1 drop). When the solution was poured into water 1-*benzoyl*-2 : 4 : 5-*triphenyl*cyclo*pentene* separated (0·18 g.) and formed colourless prisms, m. p. 182°, from aqueous alcohol and from acetone [Found : C, 89·85; H, 6·0; *M*, 415 (Rast). $C_{30}H_{24}O$ requires C, 90·0; H, 6·0%; *M*, 400·5]. It reacted with 0·27 mole of permonophthalic acid in 21 days at room temperature.

(b) *With* 3 : 5-*dinitrobenzoyl chloride and pyridine.* To 3 : 5-dinitrobenzoyl chloride prepared from 3 : 5-dinitrobenzoic acid (0·5 g.), thionyl chloride (10 ml.), and pyridine (1 ml.), (±)-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione (0·25 g.) and pyridine (2·5 ml.) were added and the mixture was heated at 100° for 30 minutes. The dark product was washed with water and sodium hydrogen carbonate solution and after five crystallisations from alcohol formed straw-coloured prisms, m. p. 179·5—180°, raised to 182° on admixture with the above product of m. p. 182°.

(c) *With sodium ethoxide.* (±)-1 : 3 : 4 : 6-Tetraphenylhexane-1 : 6-dione (2·5 g.), suspended in 95% alcohol (100 ml.), was added to a solution prepared from sodium (2 g.) and alcohol (30 ml.), and was boiled for 10 minutes. After 12 hours the solution was neutralised with acetic acid, and hot water added. On cooling, the product separated and on fractional crystallisation from alcohol formed long colourless prisms, m. p. 123° (1·7 g.), and colourless prisms, m. p. 182° (0·4 g.). The first compound, originally described by Conant and Cutter (*loc. cit.*), is now believed to be 1-benzoyl-2 : 3 : 5-triphenyl*cyclo*pentene, while the second was identical with the 1-benzoyl-2 : 4 : 5-triphenyl*cyclo*pentene described above (m. p. and mixed m. p.). When the time of reaction was reduced from 10 to 2 minutes, only 0·6 g. of the isomer of m. p. 123° was obtained, but 1·5 g. of the isomer of m. p. 182°.

When 1-benzoyl-2 : 4 : 5-triphenyl*cyclo*pentene, m. p. 182°, was treated similarly with sodium ethoxide solution, similar mixtures of the two isomers were obtained and separated by fractional crystallisation from alcohol.

Bromination of 1-*Benzoyl*-2 : 4 : 5-*triphenyl*cyclo*pentene*.—1-Benzoyl-2 : 4 : 5-triphenyl*cyclo*pentene (0·3 g.) in acetic acid (30 ml.) was treated with bromine (0·25 ml.) and warmed on the steam-bath for 10 minutes. On addition of water the dibromide separated (0·17 g.) and formed yellow needles, m. p. 178°, from aqueous alcohol (Found : C, 64·4; H, 3·85; Br, 29·0. Calc. for $C_{30}H_{22}OBr_2$: C, 64·5; H, 4·0; Br, 28·6%). This compound was also obtained by similar treatment of (±)-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione.

Bromination of 1-*Benzoyl*-2 : 3 : 5-*triphenyl*cyclo*pentene*.—1-Benzoyl-2 : 3 : 5-triphenyl*cyclo*pentene (0·2 g.), brominated as above, gave a *monobromide* which formed yellow needles, m. p. 193°, from alcohol (Found : Br, 15·5. $C_{30}H_{23}OBr$ requires Br, 16·7%).

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